

CLAIMS

What is claimed is:

1. A method of manufacturing a drug eluting implantable medical device, comprising exposing a coating of the device to charged particles for a duration, the coating comprising a polymer and an active agent.
2. The method of Claim 1, wherein exposing the coating comprises directing one or more beams of charged particles to the coating.
3. The method of Claim 2, wherein two beams of charged particles are directed to the coating, and wherein the beams are directed to the coating simultaneously.
4. The method of Claim 2, wherein two beams of charged particles are directed to the coating, and wherein the beams are directed to the coating sequentially.
5. The method of Claim 2, wherein two beams of charged particles are directed to the coating, and wherein a first beam comprises a first type of charged particles and a second beam comprises a second type of charged particles different from the first type.
6. The method of Claim 1, wherein the energy of the charged particles is between about 20 eV and about 15 MeV.
- 20 7. The method of Claim 1, wherein the one or more beams is directed to the coating at an angle of about 20° to about 80° to the coating surface.
8. The method of Claim 1, wherein the one or more beams is directed to the coating at an angle of about 90° to the coating surface.

9. The method of Claim 1, wherein exposing the coating comprises exposing the coating to an ion plasma.

10. The method of Claim 1, wherein the charged particles are selected from the group consisting of helium, oxygen, argon, fluorine, titanium, nitrogen, 5 antimony, uranium, krypton, xenon, gold and neon.

11. The method of Claim 1, wherein the current density of the charged particles is about $0.001 \mu\text{A}/\text{cm}^2$ to about $1 \mu\text{A}/\text{cm}^2$.

12. The method of Claim 1, wherein the duration of exposure is about 1 second to about 1 hour.

10 13. The method of Claim 1, wherein the ion fluence of the charged particles is between about $10^3/\text{cm}^2$ to about $10^{16}/\text{cm}^2$.

14. The method of Claim 1, wherein the coating is exposed to the charged particles in a chamber having a chamber pressure less than atmospheric pressure.

15 15. The method of Claim 1, wherein the polymer is selected from the group consisting of an ethylene vinyl alcohol copolymer, polyurethane, poly(butyl methacrylate), poly(glycolic acid), poly(lactic acid), poly(tetrafluoro ethylene), poly(vinylidene fluoride) and poly(vinylidene fluoride-co-hexafluoropropene).

16. The method of Claim 1, wherein the coating comprises less than 20 about 2% residual fluid content (w/w) when exposed to the charged particles.

17. The method of Claim 1, wherein the active agent is selected from the group consisting of rapamycin, 40-O-(2-hydroxy)ethyl-rapamycin, 40-O-(3-hydroxy)propyl-rapamycin and 40-O-[2-(2-hydroxy)ethoxy]ethyl-rapamycin.

18. The method of Claim 1, wherein the duration is of sufficient time to modify the permeability of the polymer to the active agent.

19. The method of Claim 1, wherein the charged particles are positively charged.

5 20. The method of Claim 1, wherein the implantable medical device is a stent.

21. The method of Claim 1, further comprising exposing the coating to a fluid subsequent to exposing the coating of the device to the charged particles, the fluid capable of removing polymer fragments from the coating to provide 10 hollow channels in the coating.

22. The method of Claim 21, wherein the fluid is an etchant in an aqueous solution, the etchant selected from the group consisting of HNO₃, NaOH, KOH, HCl, Na₂CO₃, CrO₃, H₂SO₄, KMnO₄, NaOCl, and Na₂B₄O₇.

23. The method of Claim 21, wherein the fluid is an organic solvent.

15 24. The method of Claim 1, further comprising exposing the coating to a temperature equal to or greater than the glass transition temperature of the polymer in the coating subsequent to exposing the coating of the device to the charged particles to produce an amorphous polymer domain.

25. The method of Claim 1, further comprising exposing the coating to 20 a gas while exposing the coating to the charged particles.

26. The method of Claim 25, wherein the gas is selected from the group consisting of hydrogen, SO₂ and oxygen.

27. A method of manufacturing a drug eluting implantable medical device, comprising:

applying a composition to an implantable medical device, the composition including a polymer, an active agent and a solvent;

5 allowing the solvent to evaporate to form a dry coating, the dry coating comprising less than about 10% residual fluid content (w/w); and

directing a beam of charged particles to the dry polymeric coating to modify the release rate of the active agent from the coating.

28. The method of Claim 27, wherein the dry coating comprises less 10 than about 2% residual fluid content (w/w).

29. The method of Claim 27, wherein the dry coating comprises less than about 1% residual fluid content (w/w).

30. The method of Claim 27, wherein the polymer is selected from the group consisting of an ethylene vinyl alcohol copolymer, polyurethane, poly(butyl 15 methacrylate), poly(glycolic acid), poly(lactic acid), poly(tetrafluoro ethylene), poly(vinylidene fluoride) and poly(vinylidene fluoride-co-hexafluoropropene).

31. The method of Claim 27, wherein the active agent is selected from the group consisting of rapamycin, 40-O-(2-hydroxy)ethyl-rapamycin, 40-O-(3-hydroxy)propyl-rapamycin and 40-O-[2-(2-hydroxy)ethoxy]ethyl-rapamycin.

20 32. The method of Claim 27, wherein the beam is directed to only a portion of the coating along the length of the stent.

33. The method of Claim 27, further comprising forming a barrier layer over the dry coating prior to directing the beam of charged particles, the barrier layer comprising a polymer substantially free from an active agent.

34. The method of Claim 33, wherein the barrier layer is of the type that 5 substantially prevents diffusion of the active agent from the coating prior to the act of directing the beam of charged particles.

35. The method of Claim 27, further comprising forming a barrier layer over the dry coating subsequent to directing the beam of charged particles, the barrier layer comprising a polymer substantially free from an active agent.

10 36. The method of Claim 27, wherein the act of directing the beam of charged particles to the coating does not reduce the total content of the active agent in the coating.

37. The method of Claim 27, further comprising masking a portion of the coating prior to directing the beam of charged particles to eliminate or reduce 15 the exposure of charged particles to the portion of the coating covered by the mask.

38. The method of Claim 37, wherein the act of masking includes inserting a mandrel into a hollow, longitudinal body of the stent to mask the inner surface of the stent.

20 39. The method of Claim 27, further comprising exposing the dry coating to a fluid subsequent to directing the beam of charged particles to the dry coating, the fluid capable of removing polymer fragments from the coating to provide hollow channels in the coating.

40. The method of Claim 39, wherein the fluid is an etchant in an aqueous solution, the etchant selected from the group consisting of HNO₃, NaOH, KOH, HCl, Na₂CO₃, CrO₃, H₂SO₄, KMnO₄, NaOCl, and Na₂B₄O₇.

41. The method of Claim 39, wherein the fluid is an organic solvent.

5 42. The method of Claim 27, further comprising exposing the dry coating to a temperature equal to or greater than the glass transition temperature of the polymer in the coating subsequent to directing the beam of charged particles to the dry coating of the device to produce an amorphous polymer domain.

43. A method of manufacturing a drug eluting stent, comprising
10 exposing a stent to charged particles for a duration, wherein the stent comprises a body including a biodegradable polymer and an active agent.

44. A system for manufacturing a drug eluting implantable medical device, comprising:

15 a mandrel to support an implantable medical device;
a source for charged particles; and
a mask positioned in between the device and the source of charged particles to eliminate or reduce the exposure of charged particles to the portion of the device covered by the mask.

45. The system of Claim 44, wherein the mask includes a slot for
20 focusing the charged particles onto a portion of the device.

46. The system of Claim 44, wherein the mandrel is configured to rotate the device.

47. A system for directing a beam of charged particles to a drug eluting implantable medical device, comprising:

an accelerator capable of ionizing gaseous molecules and producing ion beams;

5 a gas source in communication with the accelerator and capable of producing gaseous molecules; and

an implantation chamber in communication with the accelerator, the implantation chamber including a mandrel to support an implantable medical device.

10 48. The system of Claim 47, wherein the implantation chamber further includes a mask positioned in between the device and the accelerator to eliminate or reduce the exposure of ion beams to the portion of the device covered by the mask.